An interesting aspect of this project is the constant interaction with cardiologists, and the need to improve:

- our knowledge and the treatment of electrical cardiac pathologies
- the exploitation of all available electrical signals

The overall objectives of Carmen pertain both to the fields of numerical sciences, and to medical sciences through close collaborative research. The objectives in numerical sciences concern the progress to be made on data-and image-based modeling of cardiac electrophysiology, and model-based inverse reconstruction or interpretation of electrical signals. The goal in medical sciences is to contribute to the objectives of LIRYC concerning atrial fibrillation, sudden cardiac death due to ventricular fibrillation, and heart failure. Software tools are important for the success of this research.

**Context**

**Scientific priorities:** Integrative computational medicine, bridging time and space scales

**Scientific Research context:**

Cardiac arrhythmia are among the most important causes of death in the world. Arrhythmia are caused by a malfunctioning of the electrical activation system of the heart, a complex multilevel biological system that relies on the interaction of about 20 different types of current-generating molecules in the membrane of each of the heart's 2 billion muscle cells. While most arrhythmia affect elderly patients, sudden unexpected cardiac death also occurs in young, apparently healthy subjects. The cause can be genetic or toxin-related, but in most cases remains elusive. However, in many cases abnormalities in the electrocardiogram (ECG) can be a warning sign. Diagnosis and risk assessment are currently based on a small number of syndromes, defined in terms of typical ECG morphologies. The purpose of the present work is to develop a diagnosis system based on the actual mechanism of the arrhythmia and the related ECG abnormalities in each individual patient. The work will be performed in collaboration with cardiologists from the IHU LIRYC and Haut-Lévêque cardiology hospital in Bordeaux – one of the world's most experienced centers in this area. This collaboration provides us with the necessary medical background and with a wealth of medical imaging data and internal as well as external ECGs, measured with hundreds of electrodes, from a group of patients who have been diagnosed with sudden-death syndromes.

**Assignment**

To investigate different hypotheses to explain arrhythmia and ECG abnormalities in individual patients we propose a numerical modeling approach using patient-tailored models of the heart and torso. Model geometries will be based on high-resolution computed tomography data. Simulations will be performed with a reaction-diffusion model of cardiac electrophysiology. The reaction term is a complex nonlinear function of about 20 variables per model node, governed by a set of coupled ordinary differential equations. The diffusion takes place in an inhomogeneous anisotropic domain representing the cardiac muscle and surrounding tissues. The simulations use a heart model in terms of about 30 million nodes and will be performed with an existing framework on 1000 to 2000 cores of one of the national high-performance computing systems (OCCigen, Curie, Turing), using a renewable allocation of currently 10M core-hours per year. Some work is foreseen to adapt the existing code to the new requirements of the study.

The challenge of the study is to efficiently fit the numerous physiological parameters of the model to the available data, both during normal and abnormal cardiac rhythms. This will require innovative use of optimization methods and development of appropriate model reduction methods. For these aspects we rely on a large experience in the area of cardiac inverse modeling in our team [4].

An interesting aspect of this project is the constant interaction with cardiologists, and the need to...
communicate with them in terms that they can relate to from their medical background [5]. Specific guidance from interdisciplinary scientists is foreseen to help with this aspect.

The project builds on the CEMPACK, MUSIC, and CEPS software developed or co-developed by our team, and previous work on tissue homogenization approaches (PhD A Davidovic). It further takes place in relation to an ongoing project to simulate the cardiac muscle at the cellular scale (PhD P-E Bécue) and a collaboration with the STORM team to develop code that will leverage the upcoming heterogeneous (CPU-GPU) machines at the computing centers and that should ultimately allow simulations with a much higher level of detail using near-exascale computing.

**Main activities**

**Keywords:** cardiology, HPC, multiscale modeling, optimization, patient-tailored medicine

**References:**


**Skills**

**Required knowledge and background:**

For this interdisciplinary project the candidate will need knowledge in computational science, informatics, and physiology. The expected profile is a PhD in numerical science, informatics, or a related discipline, with an interest in biomedical applications and the willingness to learn about the physiological and cardiological aspects of the study. Previous work in cardiac electrophysiology is an advantage.

**Benefits package**

- Subsidised catering service
- Partially-reimbursed public transport

**Remuneration**

2653€ / month (before taxes)